

AMENDMENT

Please amend the above-identified application as follows.

IN THE CLAIMS:

Please cancel claims 1-8 without prejudice and amend the remaining claims as follows.

9-11. Cancelled

12 (Currently Amended). A method of eliciting an immune response treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon in vivo administration to said mammal.

13
13 (Original). The method of claim 12 wherein the herpesvirus is selected from the group consisting HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

14 (Original). The method of claim 13 wherein the herpesvirus is HSV-1 or HSV-2.

15 (Original). The method of claim 14 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP 27.

16 (Currently amended). A method of eliciting an immune response treating herpetic stromal keratitis in a mammal, the method comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein

essential for viral genome replication to render the herpesvirus replication defective. The method of claim 12 wherein the mammal is in need of treatment for herpetic stromal keratitis.

17 (Currently Amended). A method of treating an immunomodulatory disease a mammal ~~in need thereof~~ comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective, ~~said mutant herpesvirus having an ability to effect a subclass shift of IgG2a/IgG and induce an immunological protective effect upon administration.~~

11 contd -
18 (Currently Amended). A method of eliciting an immune response treating herpetic stromal keratitis ~~treating an immunomodulatory disease~~ in a mammal, ~~in need thereof~~ the method comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective, ~~said mutant herpesvirus having an ability to induce production of IFN- γ upon administration.~~

19 (Original). The method of claim 18 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

20 (Original). The method of claim 19 wherein the herpesvirus is HSV-1 or HSV-2.

21 (Original). The method of claim 20 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP 27.

22. Cancelled.

23-30. Cancelled

31 (Currently Amended). A vaccine in a pharmaceutically accepted carrier comprising:

~~a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective immune response in a mammal vaccinated with said herpesvirus; wherein,~~

~~said herpes virus being characterized by a mutation in at least one gene encoding a protein essential for viral genome replication of said herpesvirus, thereby; and,~~

rendering the virus genome replication defective; and,

~~the herpesvirus comprising one or more heterologous genes; wherein,~~

~~the mutated herpesvirus is capable of infecting a mammalian cell and of eliciting an immune response to heterologous gene products in a mammal vaccinated with the herpesvirus.~~

32-35. Cancelled

36 (Previously Amended). A vaccine comprising a mutated herpesvirus capable of infecting a mammalian cell; ~~and of eliciting a protective immune response upon administration;~~

~~said herpesvirus comprising a mutation in one or more early genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective; and,~~

~~encodes one or more heterologous genes~~

~~said herpesvirus comprising one or more heterologous genes encoding heterologous gene products; wherein,~~

the mutated herpesvirus is capable of infecting a mammalian cell and of eliciting an immune response to the heterologous gene products in a mammal vaccinated with said herpesvirus.

37-40. Cancelled

Cancelled 41 (Currently Amended). A method of inducing an immune response against herpesvirus in a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective and further encoding ~~eneodes~~ one or more heterologous genes.

J 41-49. Cancelled

Please add the following new claims, numbered from the last entered claim, claim 49.

50 (New). An immunogenic composition comprising a pharmaceutically acceptable carrier and a mutated herpesvirus capable of infecting a mammalian cell and of eliciting an immune response in a mammal immunized with the composition, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication.

51 (New). The immunogenic composition of claim 50, wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.

52 (New). The immunogenic composition of claim 51, wherein the herpesvirus is HSV-1 or HSV-2.

53 (New). The immunogenic composition of claim 51, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding ICP8 comprises a deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

54 (New). The immunogenic composition of claim 51, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding UL5 comprises a deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

55 (New). The immunogenic composition of claim 51, wherein the gene encoding UL5 comprises a deletion mutation and the gene encoding ICP8 comprises a deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

56 (New). The immunogenic composition of claim 55, wherein the herpesvirus is HSV-1 or HSV-2.

57 (New). A method of eliciting an immune response in a mammal, the method comprising administering to the mammal an immunogenic composition comprising a mutated herpesvirus capable of infecting a mammalian cell and eliciting an immune response, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutations render the herpesvirus incapable of replication.

58 (New). The method of claim 57, wherein said herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.

59 (New). The method of claim 57, wherein said herpesvirus is HSV-1 or HSV-2.

60 (New). The method of claim 57, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding ICP8 comprises a deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

61 (New). The method of claim 57, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding UL5 comprises deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

62 (New). The method of claim 57, wherein the gene encoding UL5 comprises a deletion mutation and the gene encoding ICP8 comprises a deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

63 (New). A method of treating a mammal to elicit an immunogenic response, the method comprising administering to the mammal an effective amount of an immunogenic composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5; or in a corresponding early gene in a non-HSV-1 herpesvirus, thereby, the mutations render the herpesvirus incapable of replication, and the mutant herpesvirus induces an immunogenic effect upon *in vivo* administration to the mammal.

64 (New). The immunogenic composition of claim 63 further comprising a mutation in at least two of the genes.

65 (New). The immunogenic composition of claim 63 further comprising a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

66 (New). The method according to claim 63, wherein the herpesvirus contains a mutation in at least two of the genes.

67 (New). The method according to claim 63, wherein the herpesvirus contains a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

68 (New). An immunogenic composition comprising a pharmaceutically acceptable carrier and a replication defective herpesvirus which expresses a heterologous protein, wherein said herpesvirus is characterized by a mutation in at least one gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5 or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication.

69 (New). The immunogenic composition of claim 68, wherein the herpesvirus is HSV-1, HSV-2, VZV, EBV, HHV-6 or HHV-7.

70 (New). The immunogenic composition of claim 68, wherein the protein essential for replication is encoded by an immediate early gene or an early gene.

71 (New). The immunogenic composition of claim 70, wherein the protein is HSV-1 ICP-27.

72 (New). The immunogenic composition of claim 70, wherein said protein is HSV-1 or HSV-2 ICP-8.

73 (New). The immunogenic composition of claim 68, wherein said herpesvirus is characterized by a mutation in two or more genes encoding HSV-1, ICP27;

HSV-1, ICP8; or HSV-1, UL5 or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication.

74 (New). The immunogenic composition of claim 73, wherein said proteins for replication are encoded by an immediate early or early genes.

75 (New). The immunogenic composition of claim 73, wherein said genes encode ICP8 and ICP 27.

76 (New). The immunogenic composition of claim 6, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding ICP8 comprises a deletion mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

77 (New). The immunogenic composition of claim 73, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding UL5 comprises a deletion mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

78 (New). The immunogenic composition of claim 73, wherein the gene encoding UL5 comprises a deletion mutation and the gene encoding ICP8 comprises a deletion mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

79 (New). The immunogenic composition of claim 73, wherein the herpesvirus expressing the heterologous protein is HSV-1 or HSV-2.

80 (New). The immunogenic composition of claim 79, wherein the heterologous protein is an immunogenic protein from a virus, bacteria, fungi or parasite.

81 (New). The immunogenic composition of claim 80, wherein the immunogenic protein is from an RNA or DNA virus.

82 (New). The immunogenic composition of claim 81, wherein the immunogenic protein is from a Human Immunodeficiency Virus (HIV).

83 (New). The immunogenic composition of claim 82, wherein the immunogenic protein elicits a B- and/or T-cell immune response.

84 (New). A method of eliciting an immune response in a mammal, the method comprising administering to the mammal an immunogenic composition comprising a mutated herpesvirus, expressing a heterologous protein and is capable of infecting a mammalian cell and eliciting an immune response, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutated herpesvirus is rendered incapable of replication.

85 (New). The method of claim 84, wherein the herpesvirus expressing the heterologous protein is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.

86 (New). The method of claim 84, wherein the herpesvirus expressing the heterologous protein is HSV-1 or HSV-2.

87 (New). The method of claim 84, wherein the gene encoding ICP27 comprises a nonsense mutation and the gene encoding ICP8 comprises a deletion mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

88 (New). The immunogenic composition of claim 84, wherein the heterologous protein is an immunogenic protein from a virus, bacteria, fungi or parasite.

89 (New). The immunogenic composition of claim 84, further comprising a mutation in at least two of the genes.

90 (New). The immunogenic composition of claim 84, further comprising a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

91 (New). A method of treating a mammal to elicit an immunogenic response, the method comprising administering to the mammal an effective amount of an immunogenic composition comprising a mutated herpesvirus expressing a heterologous protein in a pharmaceutically acceptable carrier, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; HSV-1, ICP8; or HSV-1, UL5; or in a corresponding early gene in a non-HSV-1 herpesvirus, thereby, the mutated herpesvirus is rendered incapable of replication, and the mutant herpesvirus induces an immunogenic effect upon *in vivo* administration to the mammal.

92 (New). The method according to claim 91, wherein the herpesvirus contains a mutation in at least two of the genes and expresses a heterologous protein.

93 (New). The method according to claim 91, wherein the herpesvirus contains a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

94 (New). The method according to claim 91, wherein the herpesvirus contains a mutation in at least two of the genes.

95 (New). The method according to claim 91, wherein the herpesvirus contains a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

95 (New). The method of claim 91, wherein the heterologous protein is an immunogenic protein from a virus, bacteria, fungi or parasite.

J' concid.

96 (New). The method according to claim 91, wherein the *in vivo* immunogenic effect in a mammal comprises a B- cell and/or T cell response.